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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/462,089	05/01/2000	Michael Kerin McNamara	017227/0154	4665

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EXAMINER	
HUYNH, PHUONG N	
ART UNIT	PAPER NUMBER
1644	19

DATE MAILED: 12/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/462,089	Applicant(s) MCNAMARA, MICHAEL KERIN	
	Examiner " Neon" Phuong Huynh	Art Unit 1644	

-- The MAILING DATE of this communication app ars on th cover she t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 September 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-8 are pending.

2. In view of the amendment filed 9/27/02, the following rejections remain.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of (1) *any* composition for use in eliciting an effective immune response to LHRH said composition comprising *any* LHRH-diphtheria toxoid conjugate absorbed to *any* ionic polysaccharide wherein said LHRH "comprises" a C-terminal fragment of at least *any* five amino acids; (2) *any* composition for use in eliciting an effective immune response to LHRH said composition comprising *any* LHRH-diphtheria toxoid conjugate absorbed to an ionic polysaccharide wherein said LHRH "comprises" a C-terminal fragment of at least *any* five amino acids wherein said ionic polysaccharide is DEAE-dextran; (3) *any* composition for use in eliciting an effective immune response to LHRH said composition comprising *any* LHRH-diphtheria toxoid conjugate absorbed to an ionic polysaccharide wherein said LHRH "comprises" a C-terminal fragment of at least *any* five amino acids wherein said LHRH is *any* "LHRH 2-10 form"; (4) *any* composition for use in eliciting an effective immune response to LHRH said composition comprising *any* LHRH-diphtheria toxoid conjugate absorbed to an ionic polysaccharide wherein said LHRH "comprises" a C-terminal fragment of at least *any* five amino acids wherein said LHRH is *any* "modified LHRH 2-10 form"; (5) *any* pharmaceutical composition comprising *any* LHRH-diphtheria toxoid conjugate absorbed to *any* ionic polysaccharide together with one or more pharmaceutically acceptable carriers and/or diluents wherein said LHRH "comprises" *any* C terminal fragment of at least *any* five amino acids; (6) *any* pharmaceutical composition comprising *any* LHRH-

diphtheria toxoid conjugate absorbed to *any* ionic polysaccharide together with one or more pharmaceutically acceptable carriers and/or diluents wherein said LHRH "comprises" *any* C terminal fragment of at least *any* five amino acids wherein said ionic polysaccharide is DEAE-dextran; (7) *any* pharmaceutical composition comprising *any* LHRH-diphtheria toxoid conjugate absorbed to *any* ionic polysaccharide together with one or more pharmaceutically acceptable carriers and/or diluents wherein said LHRH "comprises" *any* C terminal fragment of at least *any* five amino acids wherein said LHRH is *any* "LHRH 2-10 form", (8) *any* pharmaceutical composition comprising *any* LHRH-diphtheria toxoid conjugate absorbed to *any* ionic polysaccharide together with one or more pharmaceutically acceptable carriers and/or diluents wherein said LHRH "comprises" *any* C terminal fragment of at least *any* five amino acids wherein said LHRH is *any* "modified LHRH2-10 form" for controlling fertility by eliciting antibody immune response to LHRH.

The specification discloses only a composition or a pharmaceutical composition comprising a LHRH of SEQ ID NO: 2 or 4 conjugated to diphtheria toxoid and adjuvant with DEAE dextran for inducing a strong antibody to LHRH for inhibition of fertility. The specification defines derivatives includes fragments, parts, portions, chemical equivalent, mutants, homology, analogs, fusion protein (See page 5, lines 17-18). Chemical equivalents of LHRH may not derived from LHRH but may share certain similarities. The specification further defines "derivatives" may be derived from insertion, deletion, or substitution of amino acids (page 6).

Other than the specific LHRH peptide selected from the group consisting of SEQ ID NO: 1-4 mentioned above conjugated to diphtheria toxoid for a contraceptive vaccine, there is inadequate written description about the structure associated with function of *any* LHRH "comprises" a C-terminal fragment of at least five amino acids because the term "comprises" is open-ended. It expands the LHRH to include additional amino acid at either or both ends, much less having the same function as SEQ ID NO: 2 and 4. There is inadequate written description about the additional undisclosed amino acid residues to the LHRH fragment that is conjugated to diphtheria in the claimed composition.

With regard to *any* LHRH 2-10 form, and *any* LHRH is *any* modified LHRH 2-10 form conjugated to diphtheria toxoid, the "LHRH 2-10 form" without SEQ ID NO: has no structure, much less function. Since the "LHRH 2-10 form" is not adequately describe, it follows that the modified form of the inadequate describe "LHRH 2-10 form" is not sufficiently disclosed.

Finally, the specification discloses only four modified form of LHRH represent by SEQ ID NO: 1-4 from human only. Given the lack of a written description of *any* additional representative species of LHRH2-10 form, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicants' arguments filed 9/27/02 have been fully considered but are not found persuasive.

Applicants' position is that (1) the claims set forth with structural detail, (2) the Examiner claims 1 and 5 have been amended to recite wherein said LHRH comprises a C-terminal fragment of at least five amino acids".

However, there is inadequate written description about the structure associated with function of *any* LHRH "comprises" a C-terminal fragment of at least five amino acids because the term "comprises" is open-ended. It expands the LHRH to include additional amino acid at either or both ends as long as the LHRH contains a C-terminal fragment of five amino acids. Further, it is not clear the source of that "C-terminal fragment of five amino acids". Even if composition comprising a LHRH-diphtheria toxoid conjugate adsorbed to an ionic polysaccharide wherein said LHRH comprises a C-terminal fragment of at least five amino acid from LHRH, the term "comprises" is still open-ended. There is inadequate written description about the additional undisclosed amino acid residues to the LHRH fragment that is conjugated to diphtheria in the claimed composition. With regard to the insufficient written description about the structure associated with function of *any* LHRH 2-10 form, and *any* LHRH is *any* modified LHRH 2-10 form conjugated to diphtheria toxoid, the "LHRH 2-10 form" without SEQ ID NO: has no structure, much less function. Since the "LHRH 2-10 form" is not adequately describe, it follows that the modified form of the inadequate describe "LHRH 2-10 form" is not sufficiently disclosed. Finally, the specification discloses only four modified form of LHRH represent by SEQ ID NO: 1-4 from human only. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus,

Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 5,378,688 (of record, Jan 1995, PTO 892) or Sad *et al* (of record, Immunology74: 223-227 (1991, PTO 892) each in view of US Pat No. 5,614,487 (March 1997, PTO 892) or US Pat No. 5,403,586 (of record, April 1995, PTO 892).

The '688 patent teaches a pharmaceutical composition comprising a LHRH-diphtheria toxoid conjugate for a contraceptive vaccine (See column 5, last paragraph bridging column 6, first paragraph, Claim 1 of '688 patent, in particular). The '688 patent teaches modified form of LHRH or analog such as the ones in Table on column 5, and a method of making said LHRH conjugate (See column 16, last paragraph, in particular). The '688 patent further teaches that conjugation of LHRH to toxin is useful for destroying the gonadotrophs of the animal's anterior pituitary gland for sterilizing the animal (See abstract, in particular). Claim 5 is included in this rejection because the '688 patent teach modified LHRH and analog of LHRH that comprises the C-terminal fragment of at least five amino acids of LHRH and amidated (having the NH_2 group) at the C-terminus (See column 8, lines 59-68, in particular), which is consistent with the definition of LHRH 2-10 form as disclosed on page 8 lines 6-9 of instant specification. Claims 4 and 8 are included in this rejection because the '688 patent further teaches modified form of LHRH 2-10 such as having amino acid substitution at the 6 and 10 positions of the LHRH peptide regardless of the nomenclature (See column 5, Superagonists, column 9, lines 25-41, in particular). The reference LHRH 2-10 form includes the LHRH fragment "comprises" a C-terminal fragment of at least five amino acids of LHRH.

Sad *et al* teach a pharmaceutical composition comprising a GnRH, also known as LHRH, conjugated to diphtheria toxoid (DT) in alumn (See page 224, column 1, first three full paragraphs, in particular). The reference GnRH is a decapeptide (full length), which includes the

claimed LHRH fragment of at least five amino acids of the C terminal of LHRH (See page 223, column 2, Material and Methods, in particular). The term "comprising" is open-ended. It expands the claimed fragment to include the reference GnRH.

The claimed invention in claims 1 and 6 differs from the references only by the recitation of said composition comprises an ionic polysaccharide wherein said polysaccharide is DEAE dextran.

The '487 patent teaches a drug carrier such as dextran which is a polymer of glucose, also known as polysaccharide, containing vicinal diols that can be used for the sustained release of virtually any biologically active polypeptide (See abstract, column 3, lines 58-64, column 4, lines 15-30, in particular). The '487 patent teaches that dextrans have the advantages as drug carrier because of (1) high water solubility (ionic), (2) a well-defined and repetitive chemical structure, yielding many potential sites for binding or conjugation, (3) their availability in different molecular weight forms of from about $2x10^3$ to 10^6 and (4) low toxicity and inert (low pharmacological activity) (See column 4, lines 17-23, in particular).

The '586 patent teaches suitable adjuvant for the vaccination of animals and humans includes such as DEAE-dextran in a pharmaceutical composition comprising LHRH-TRATP fusion protein for inhibiting or controlling the reproductive function in vertebrate host (See column 5, lines 48-62, Abstract, in particular). The '586 patent further teaches the vaccine composition may combined together with other carrier, diluents, excipient and/or adjuvant such as sterile water, Ringer's solution and isotonic sodium chloride solution (See column 5, 14-47, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the diphtheria toxoid conjugate for a contraceptive vaccine as taught by the '688 patent or substitute the alum as taught by Sad et al with the drug carrier such as polysaccharide dextran as taught by the '487 or the '586 patents.

One having ordinary skill in the art at the time the invention was made would have been motivated to do this because the '487 patent teaches the use of dextrans for the sustained release of virtually any biologically active polypeptide and dextrans have the advantages as drug carrier because of (1) high water solubility (ionic), (2) a well-defined and repetitive chemical structure, yielding many potential sites for binding or conjugation, (3) their availability in different molecular weight forms of from about $2x10^3$ to 10^6 and (4) low toxicity and inert (low pharmacological activity) (See column 4, lines 17-23, Abstract, in particular). The '586 patent

teaches polysaccharide such as DEAE-dextran is suitable adjuvant for the vaccination of animals and humans (See column 5, lines 48-62, Abstract, in particular).

Applicants' arguments filed 9/27/02 have been fully considered but are not found persuasive.

Applicants' position is that (1) there is no teaching or suggestion in the '688 patent or Sad et al to administer an LHRH-diphtheria toxoid conjugate in combination with an ionic polysaccharide to elicit an effective immune response. (2) Amended claims 1 and 5 are directed to either a composition for in eliciting an effective immune response to LHRH (claim 1) or a pharmaceutical composition (claim 5) comprising a LHRH-diphtheria toxoid conjugate absorbed on an ionic polysaccharide wherein said LHRH comprises a C-terminal fragment of at least five amino acids. (3) The '688 patent does not teach or suggest the reference composition would be useful for inducing an immune response to a suitably formulated hormone antigen. (4) Sade et al teach both stimulation and suppression of an immune response against GnRH. (5) The Examiner is using improper hindsight reconstruction in asserting that the prior art provided the requisite motivation to use an LHRH-diphtheria toxoid conjugate in combination with an ionic polysaccharide to elicit an effective immune response to LHRH.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicant's argument that there is no teaching or suggestion in the '688 patent or Sad et al to administer an LHRH-diphtheria toxoid conjugate in combination with an ionic polysaccharide "to elicit an effective immune response", a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so

long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

7. The following new ground of rejection is necessitated by the amendment filed 9/27/02.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for (1) a composition for use in eliciting an effective immune response to LHRH said composition comprising a LHRH-diphtheria toxoid conjugate adsorbed to an ionic polysaccharide wherein LHRH consisting of a C-terminal fragment of LHRH of at least five amino acids selected from the group consisting of SEQ ID NO: 2-4; (2) the said composition wherein said ionic polysaccharide is DEAE-dextran; (3) the said composition wherein the LHRH is LHRH 2-10 form of SEQ ID NO: 2; (4) the said composition wherein the LHRH is the modified LHRH 2-10 form of SEQ ID NO: 2 conjugated to diphtheria toxoid; (5) a pharmaceutical composition comprising a LHRH-diphtheria toxoid conjugate absorbed to an ionic polysaccharide together with one or more pharmaceutically acceptable carriers and/or diluents wherein said LHRH consisting of a C-terminal fragment of LHRH of at least five amino acids selected from the group consisting of SEQ ID NO: 2-4; (6) the said pharmaceutical composition wherein said ionic polysaccharide is DEAE-dextran; (7) the said pharmaceutical composition wherein the LHRH is LHRH 2-10 form of SEQ ID NO: 2; (8) the said pharmaceutical composition wherein the LHRH is the modified LHRH 2-10 form of SEQ ID NO: 8, **does not** reasonably provide enablement for (1) *any* composition for use in eliciting an effective immune response to LHRH said composition comprising *any* LHRH-diphtheria toxoid conjugate absorbed to *any* ionic polysaccharide wherein said LHRH "comprises" a C-terminal fragment of at least *any* five amino acids; (2) *any* composition for use in eliciting an effective immune response to LHRH said composition comprising *any* LHRH-diphtheria toxoid conjugate absorbed to an ionic polysaccharide wherein said LHRH "comprises" a C-terminal fragment of at

least *any* five amino acids wherein said ionic polysaccharide is DEAE-dextran; (3) *any* composition for use in eliciting an effective immune response to LHRH said composition comprising *any* LHRH-diphtheria toxoid conjugate absorbed to an ionic polysaccharide wherein said LHRH "comprises" a C-terminal fragment of at least *any* five amino acids wherein said LHRH is *any* "LHRH 2-10 form"; (4) *any* composition for use in eliciting an effective immune response to LHRH said composition comprising *any* LHRH-diphtheria toxoid conjugate absorbed to an ionic polysaccharide wherein said LHRH "comprises" a C-terminal fragment of at least *any* five amino acids wherein said LHRH is *any* "modified LHRH 2-10 form"; (5) *any* pharmaceutical composition comprising *any* LHRH-diphtheria toxoid conjugate absorbed to *any* ionic polysaccharide together with one or more pharmaceutically acceptable carriers and/or diluents wherein said LHRH "comprises" *any* C terminal fragment of at least *any* five amino acids; (6) *any* pharmaceutical composition comprising *any* LHRH-diphtheria toxoid conjugate absorbed to *any* ionic polysaccharide together with one or more pharmaceutically acceptable carriers and/or diluents wherein said LHRH "comprises" *any* C terminal fragment of at least *any* five amino acids wherein said ionic polysaccharide is DEAE-dextran; (7) *any* pharmaceutical composition comprising *any* LHRH-diphtheria toxoid conjugate absorbed to *any* ionic polysaccharide together with one or more pharmaceutically acceptable carriers and/or diluents wherein said LHRH "comprises" *any* C terminal fragment of at least *any* five amino acids wherein said LHRH is *any* "LHRH 2-10 form", (8) *any* pharmaceutical composition comprising *any* LHRH-diphtheria toxoid conjugate absorbed to *any* ionic polysaccharide together with one or more pharmaceutically acceptable carriers and/or diluents wherein said LHRH "comprises" *any* C terminal fragment of at least *any* five amino acids wherein said LHRH is *any* "modified LHRH2-10 form" for controlling fertility by eliciting antibody immune response to LHRH. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient

to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only a composition or a pharmaceutical composition comprising a LHRH of SEQ ID NO: 2 or 4 conjugated to diphtheria toxoid and adjuvant with DEAE dextran for inducing a strong antibody to LHRH for inhibition of fertility. The specification defines derivatives includes fragments, parts, portions, chemical equivalent, mutants, homology, analogs, fusion protein (See page 5, lines 17-18). Chemical equivalents of LHRH may not derived from LHRH but may share certain similarities. The specification further defines "derivatives" may be derived from insertion, deletion, or substitution of amino acids (page 6).

The specification does not teach *any* LHRH fragment comprising any additional amino acids having the same functions and activity as SEQ ID NO: 1-4. The specification does not teach how to make and use *any* composition or pharmaceutical comprising *any* LHRH-diphtheria toxoid conjugate wherein said LHRH "comprises" *any* C-terminal fragment of any protein of at least *any* five amino acids for eliciting *any* immune response. The term "comprises" is open-ended. It expands the LHRH fragment to include additional amino acid residues at either or both ends. There is insufficient guidance with regard to the additional undisclosed amino acid to be added to either or both ends, much less having the same function as SEQ ID NO: 1-4, in turn, would be useful for eliciting antibody response to inhibit reproductive functions. There are insufficient in vivo working examples demonstrating any composition or pharmaceutical composition comprising any LHRH-diphtheria toxoid conjugate wherein said LHRH is any derivatives, any portions, any chemical equivalent, any mutants, any homology, any analogs, and any fusion protein are effective for eliciting antibody response to LHRH, in turn, useful as a contraceptive.

Ngo *et al* teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (See Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495).

Kuby *et al* teach that immunizing a peptide versus a full-length protein may result in **antibody specificity** that differs from antibody specificity directed against the native full-length polypeptide. Without the specific amino acid residues, it is unpredictable which undisclosed LHRH-conjugate in a composition would generate antibody that has the binding specificity for

LHRH. In the absence of guidance as to what alterations would result in LHRH-diphtheria toxoid conjugate that retains the same functions and generating antibody having the same binding specificity as antibody to LHRH, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

Abaza *et al* teach that even a single amino acid substitution outside the antigenic site can exert drastic effects on the reactivity of a protein with monoclonal antibody against the site (See abstract, in particular). Given the indefinite number of undisclosed "LHRH comprises any C-terminal fragment of at least five amino acids", it is unpredictable which undisclosed "LHRH comprises any C-terminal fragment of at least five amino acid" would be effective for a composition for use in eliciting antibody immune response to LHRH, in turn, has contraceptive functions.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

10. No claim is allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

13. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
December 16, 2002

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600